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ABSTRACTS FROM THE ORIGINAL PAPERS.

The Constitution of Kojic Acid, a γ-Pyrone Derivative Formed by Aspergillus Oryzae from Carbohydrates.

By T. Yabuta.

Previous work (J. Chem. Soc. Tokyo, 1916, **37**, 1185, 1234) has shown that kojic acid (I) is probably the alcohol corresponding with comenic acid. Interconversion by oxidation of kojic acid or reduction of comenic acid has not been accomplished, but both compounds furnish the same *4*:*5*-dihydroxy-2-methylpyridine. Kojic acid on treatment with thionyl chloride yields *5*-hydroxy-2-chloromethyl-γ-pyrone, needles, m. p. 119-121°, and on reduction with zinc dust and acetic acid gives allomaltol (*5*-hydroxy-2-methyl-γ-pyrone), prisms, m. p. 166°. Allomaltol is distinct from maltol (Brand, Ber., 1894, **27**, 806) and from isomaltol (Backe, Compt. rend., 1910, **150**, 540; **151**, 78), the distinction being confirmed by the preparation of the following derivatives. Allomaltol methyl ether (*5*-methoxy-2-methyl-γ-pyrone), prisms, m. p. 70–71°, b. p. (approx.) 93°/0.1 mm.; benzoylallomaltol (*3*-benzoyloxy-*6*-methyl-γ-pyrone), prisms, m. p. 128–129°; phenylcarbamate of allomaltol, NHPh. CO. $C_6H_5O_3$, plates, m. p. 186–188°; bromoallomatol (*6*-bromo-*5*-hydroxy-2-methyl-γ-pyrone), crystals, m. p. 171–175°. Benzene azoallomaltol (*6*-benzeneazo-*5*-hydroxy-2-methyl-γ-pyrone), by treating allomaltol in solution with diazobenzene acetate, forms reddish-brown needles, no definite m. p.

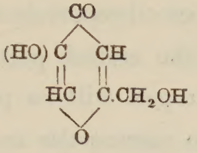
Oxidation of the following kojic acid derivatives did not give the corresponding comenic acid derivatives: monobenzoyl kojic acid; monoethyl ether of kojic acid, (*5*-ethoxy-2-hydroxy-methyl- γ-pyrone), prepared by the interaction of kojic acid, ethyl *p*-toluenesulphonate, and sodium ethoxide in alcohol, needles, m. p. 110°; *5*-ethoxy-2-hydroxymethyl-*4*-pyridine, prepared from kojic acid monoethyl ether, and isolated as the picrate, needles, m. p. 184–185°; *5*-hydroxy-2-

chloromethyl-γ-pyrone and its methyl ether; *5*-hydroxy-*2*-iodomethyl-γ-pyrone, prepared from the corresponding chloro-compound as crystalline plates; *5*-methoxy-*2*-iodomethyl-γ-pyrone, prisms, m. p. 135- 137°.

The following derivatives of comenic acid were prepared, but reduction did not give the corresponding kojic acid derivatives. Benzoylcomenic acid, prisms from alcohol, m. p. 227–228°; methyl ether of comenic acid, prisms, m. p. 280–282°; methyl ether of methyl comenate, m. p. 197°; methyl ether of ethyl comenate, m. p. 156°; the hydrochloride of the methyl ether of comenyl chloride (II), prepared by the action of thionyl chloride on comenic acid methyl ether, prisms, m. p.103°: the methyl ether of comenyl chloride, prepared from the previous compound by the action of sodium acetate, m. p. 148°: comenamide methyl ether, prepared by the action of ammonia on (II), needles, m. p. 178°. The catalytic reduction of the methyl ether of comenyl chloride by Rosenmund's method (Ber., 1918, **51**, 585; 1921, **54**, (B), 425, 638), failed owing to the instability of the pyrone nucleus. Comenamic acid methyl ether (*5*-methoxy-*4*-pyridone-2-carboxylic acid) was prepared by the action of ammonia on comenic acid methyl ether; ammonium salt, needles, m. p. 265°; hydrochloride, prisms. Thionyl chloride introduces chlorine into the *4*-position of the methyl ether, giving *4*-chloro-*5*-methoxypyridine-2-carboxylic acid chloride, which Rosenmund's method also failed to reduce. The acid chloride was converted into *4*-chloro-*5*-methoxy-pyridine-2-carboxylic acid, prisms, m. p. 209°, into the amide, needles, m. p. 207–208°, into the ethyl ester, prisms, m. p. 167°, and into the ethyl ester, prisms m. p. 140°.

Allomaltol methyl ether, prepared either by the methylation of allomaltol or by the reduction of *5*-methoxy-2-chloromethyl-*4*-pyrone, when heated with ammonia in a closed tube at 100° gives *5*-methoxy-2-methyl-4-pyridone, needles, m. p. 115°, which gives a picrate, needles, m. p. 205–206°. The dimethyl ether of kojic acid, when similarly treated, yields the corresponding pyridine derivative, which distils at 200°/1mm., and on heating with red phosphorus and hydriodic acid gives *4* : *5*-dihydroxy-2-methylpyridine, prisms, decomp. 280°. and crystallising + $1H_2O$ at low temperatures.

Comenic acid when heated with ammonia under pressure gives comenamic acid, which when treated with phosphorus pentachloride and then reduced with tin and hydrochloric acid gives the same *4* : *5*-dihydroxy-2-methylpyridine. The dihydroxy-picolines obtained thus from both acids gave on methylation the same *5*-methoxy-*1* : 2-dimethyl-*4*-pyridone ($+3H_2O$), colourless needles, m. p. 98°. This compound is also formed by treating allomaltol methyl ether with methylamine, thus confirming the position of the methyl groups. Comenamic acid on methylation gives similarly *5*-methoxy-*1*-methyl-*4*-pyridone-2-carboxylic acid ($+4H_2O$), needles, m. p. 208°.



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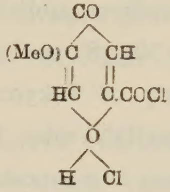

(II)

Sinomenine and Dehydrosinomenine. Parts I and II.

By Kakuji Gotō.

Sinomenine and dehydrosinomenine are alkaloids from the root of a Japanese mountain climbing plant, Sinomenum acutum, Rehd. et Wils., Menisperaceae. The first of them, sinomenine was first isolated by Katsuta Taguchi in a pure crystalline state. He named at first the alkaloid Cocculine (and afterwards Cucoline), according to the obsolute name, Cocculus diversifolius, Diels., formerly given to this plant. He analysed the alkaloid and assigned the formula $C_{17}H_{29}NO_3$ (and afterwards $C_{16}H_{20}NO_3$). Although his descriptions on the melting point, which is 158°, and on the other properties seem to be fairly well established, his formula seems unfortunately to be incorrect. (Tokyo Iji Shinshi, 1919, Dec. 13th.)

Shortly after Taguchi, J. Ishiwari published his pharmacological investigations of the alkaloid, in which some of the chemical properties are also given. (Chugai Iji Shimpo, 1920, No. 959 and 1921, No. 991.)

Succeeding Taguchi, I took up the investigation of the alkaloid and was working several years on it, when in June, 1923 a paper on the same alkaloid was read by Heizaburo Kondo and Eiji Ochiai before the Pharmaceutical Society of Japan (J. Pharm. Soc. Japan, 1923, No. 497, 511). This instigated me to publish my thitherto obtained results in July, 1923, in the Chemical Society of Tokyo (J. Chem. Soc. Japan, Vol. 44, 795, 1923). The results of the last named two authors were in accordance with those of mine in main respects, but in some points they were in advance of me and in others I. Kondo and Ochiai pointed out on the authority of a specialist that the botanical name of the plant must be Sinomenum acutum, and hence the name sinomenine is generally accepted. These two authors published the second report in Dec. 1923 (J. Pharm. Soc. Japan. 1924, No. 503, 8), and I read the second paper in May this year in the Chemical Society of Tokyo. (This report will be published soon in the journal.) Here, for brevity's sake, I wish to resume the results of my investigation, published in these two reports and ask the readers to refer to the originals, as regards the investigations of those two authors.

Isolation.

Finely sliced root of the plant is just covered with 0.5 per cent hydrochloric acid and, after standing about a week at ordinary temperature, it is filtered through cloth. The filtrate is added with concentrated solution of sodium carbonate so long as yet greyish precipitate is formed. This precipitate does not contain alkaloids appreciably, so that it is filtered off quickly. The brown alkaline solution thus obtained is shaken vigorously with chloroform three times. The alkaloids are again extracted from the chloroform solution with 0.5 per cent hydrochloric acid. The latter is concentrated under diminished pressure and on standing the hydrochlorides of sinomenine and dehydrosinomenine crystallise out directly. This process is repeated two or three times and at last the solution is decolourised with animal charcoal. The yield of raw sinomenine hydrochloride is about 0.5 per cent, mixed with a small quantity of the hydrochloride of dehydrosinomenine.

Sinomenine, its properties.

Free base melts at 159–162°. It is easily soluble in alcohol, aceton and chloroform, very little soluble in water and ether and almost insoluble in benzene and ligroin. It forms crystalline salts with hydrochloric, hydrobromic, hydroiodic and nitric acid, but the salts with sulphuric and acetic acid are not crystallisable. The hydrochloride contains two molecules of water of crystallisation and melts at 231° (incorr.). Its solubility in cold water is 4.8 per cent. Elemental analysis gave the following results. $C=69.95$, $H=7.54$, $N=4.33$; $C_{19}H_{23}NO_4$, requires

C=69.38, H=7.04, N=4.25 per cent. Cryoscopic measurement in nitrobenzene gave the molecular weight of 310. Analysis of the hydrochloride (Cl=9.93 per cent), iodomethylate (I=27.41 per cent) and chloroplatinate (Pt=18.81 per cent) gave nearly the same result.

Sinomenine is laevorotatory. Its specific rotatory power in 0.6% chloroform solution is −73°.92 (by sodium light, at 25° C). The hydrochloride is also laevorotatory.

Colour reactions of sinomenine are as follows: with conc. sulphuric acid, not coloured; with conc. nitric acid; reddish yellow; with vanadine sulphuric acid, deep green; with molybdane sulphuric acid, violet, etc.

Sinomenine is precipitated by ordinary alkaloid reagents. All these precipitates are amorphous. The chloroaurate, suspended in water, decomposes after several hours, giving dehydrosinomenine and a brown syrupy matter. Reducing property of sinomenine is remarkable. Thus it precipitates hydrate of manganese dioxide from 0.5 per cent solution of potassium permanganate. Its chloroaurate decomposes by itself on standing and metallic gold is precipitated. From 1 per cent solution of silver nitrate silver is separated on the addition of sinomenine in cold; the solution taking sometimes a reddish violet colour for a moment. Solution of sinomenine hydrochloride produces a violet colour, when added with dilute solution of ferricyanide, made alkaline with sodium carbonate, and under the favourable condition dehydrosinomenine crystallises out directly. This violet colour is taken up by chloroform in much deeper nuance and is observed even in 1 : 100,000th dilution of sinomenine. The colour in chloroform disappears on the addition of an acid or on standing overnight. In all these reactions and also by the action of ferric chloride on the solution of sinomenine hydrochloride dehydrosinomenine is formed with varying yield (see further). But sinomenine neither reduces mercuric acetate nor restores the red colour of decolourized solution of magenta with sulphurous acid.

Diazoreaction of sinomenine is beautiful. An intense red colour is produced when a few drops of 0.5 per cent solution of sinomenine made slightly acidic with hydrochloric acid, are added to an alkaline solution of diazobenzene sulphonic acid. The colour is produced even in one millionth dilution of sinomenine, thus nearly fifty times exceeding that of morphine hydrochloride in sensitiveness. This property may be taken use of in the study of the distribution of sinomenine, when injected in animal bodies.

Properties of Nitrogen and Oxygen Atoms.

Sinomenine is a tertiary base. Its aqueous solution shows a marked alkaline reaction. It was thitherto neither benzoylated, acetylated nor methylated on its nitrogen atom. It does not give Liebermann's nitroso-reaction. On the contrary, the method of Herzig and Meyer reveals the presence of one methyl group attached to the nitrogen atom (4.3%; calculated 4.56%). Monomethylamine was isolated in two cases, once in the distillation of sinomenine with zinc dust, and the other time with baryta.

Iodomethylate of sinomenine (m. p. 255° dec.) is easily formed when sinomenine and methyliodide is mixed in alcohol solution. Recrystallised from water, it contains one molecule of crystal water.

Of the four oxygen atoms contained in sinomenine, two exist as methoxyl (18.27 per cent; $2CH_3O$ require 18.85 per cent), one as carbonyl (oxim, m. p. 233°: N=8.7 per cent; $C_{15}H_{24}N_2O_4$ requires N=8.1 per cent), and the last as hydroxyl.

The existence of hydroxyl was suspected from the facts that a deep green colour is produced by sinomenine on the addition of ferric chloride and that sinomenine is easily soluble in 10 per cent caustic alkali. But it could be neither methylated with dimethylsulphate in a usual way, nor acetylated with acetylchloride or with acetylanhydride. Kondo and Ochiai showed that it could be benzoylated by heating it at 100° C with bezoylanhydride. Following their description, I could confirm the fact, the yield amounting to 30% of the alkaloid used

Benzoylsinomenine (m. p. 225°) gives no ferric chloride reaction. Diazoreaction appears very slowly with it, perhaps the reaction is produced according as benzoylsinomenine is hydrolysed. Determination of benzoyl group by the hydrolysis with caustic soda and titration, gave the number corresponding to one benzoyl group (23.98 per cent; $C_{26}H_{27}NO_5$, requires 23.55 per cent.)

Kondo and Ochiai could moreover prepare monomethylsinomenine by the action of diazomethane on sinomenine, and showed the existence of carbonyl group, independent of the hydroxyl, by converting the monomethylsinomenine into its oxime. I can not yet proceed to this point, but there is now reason to believe that sinomenine can also be methylated by dimethylsulphate to a very small extent. 10 grams sinomenine, methylated with caustic soda and dimethylsulphate, gave 0.5 gram delicate needle, which on the contrary to sinomenine, gave neither ferric chloride reaction nor diazoreaction. It dissolves in concentrated sulphuric or hydrochloric acid with beautiful blue colour, while sinomenine itself dissolves in these reagents almost colourless. Only scarcity of the yield prevented me to proceed further.

Reduction.

Sinomenine seems not to be reduced by common reducing agents such as tin and hydrochloric acid, zinc and acetic acid, or sulphuric acid, and ammonium sulphide. But it is easily hydrogenated by molecular hydrogen, using platinum black or colloidal palladium as catalyst. By the latter method, hydrosinomenine is obtained in 60 per cent yield. The results of analysis show that the substance thus obtained is formed by the addition of two atoms of hydrogen to sinomenine ($C=70.76$, $H=8.19$, $N=4.55\%$; $C_{19}H_{25}NO_4$ requires $C=68.84$, $H=7.6$, $N=4.23$ per cent).

Hydrosinomeine (m. p. 201°) is more soluble in ordinary solvents than sinomenine itself. Colour reactions and precipitation reactions are almost indentical with those of sinomenine. It shows, in particular, the ferric chloride reaction and diazoreaction. The sign of rotation is opposite, i. e. $[\alpha]_D^{24.5}=+193°.58$ in chloroform and $[\alpha]_D^{24}=+33.°06$ in weakly acidic solution. No salt of hydrosinomenine is yet obtained in crystalline form. Iodomethylate (m. p. 268° dec.) is prepared as with sinomenine. Hydrosinomenine combines with hydroxylamine (oxime m. p. 211°).

Hydrosinomenine could neither be benzoylated nor acetylated by usual methods. In an attempt to methylate it with dimethylsulphate, a larger part of hydrosinomenine was only recovered from the reaction mixture. Benzoylation with benzoylanhydride, as will be described further with sinomenine, was not successful here.

Attempts to obtain sinomenine from hydrosinomenime by the use of mild oxidising agents, such as dilute solution of pottassium permanganate or of ferricyanide and soda gave no expected result.

Bromination.

Sinomenine takes up four bromine atoms, when acted by the vapour of the latter under a bell-jar. (2 grams of sinomenine takes 2.4 grams of bromine, one bromine atom enters as hydrobromic acid, forming the salt.). From aqueous solution of sinomenine hydrochloride, yellow or brown syrupy matter is precipitated on the addition of bromine, but it was impossible to make it crystallise. As Ishiwari first indicated, bromination is more successful in glacial acetic acid, when one part of bromine is added to two parts of sinomenine hydrochloride, dissolved in the solvent. If bromine is used in a larger quantity, only syrupy matter is obtained. By careful purification, two isomers were unexpectedly isolated from this reaction product. From the content of bromine, the both seem to have the same formula $C_{19}H_{22}NO_4$ Br. The property of the both substances may be conveniently compared as follows.

	Bromsinomenine.	Isobromsinomenine.
Solubility in alcohol.	soluble in cold alcohol.	insoluble in hot alcohol.
M. P. of free bases.	153°	214°
Content of bromine.	19.91 per cent	18.99 per cent.
M. P. of the hydrobromide.	110 (with 3 Aq.). 231 (anhydrous)	229 (anhydrous).
M. P. of Iodomethylate.	80	210–211.
Ferric chloride reaction.	light green	is not produced.
Diazoreaction.	deep red	no colour is produced.
Reduction of gold chloride.	strong	very weak.
With molybdane-sulphuric acid.	deep violet	violet at first and quickly pink.
Rotatory power: free base.	$[\alpha]^{25}_{D}=-2^{\circ}.62$	$+14^{\circ}.65$
Rotatory power: hydrochloride.	$[\alpha]^{22.5}_{D}=-30^{\circ}.19$	$+51^{\circ}.79$
Yield.	80 per cent of the total.	20 per cent of the total.

As is seen from the above table, these two isomers are separated by boiling alcohol, in which isocompound is not soluble. Isobromsinomenine shows a remarkable divergence in its property from sinomenine and bromsinomenine, in as much as it gives neither ferric chloride reaction nor diazoreaction and its violet colour in Froehde's reagents turns quickly pink. From these facts it may be inferred that in isobromsinomenine the hydroxyl group might have been replaced by bromine atom. But in that case, the content of bromine must be naturally much higher.

Dehydrosinomenine.

Dehydrosinomenine, which was first prepared by me from sinomenine through mild oxidising agents, was found afterwards occurring actually in the root of the plant. As the hydrochloride of dehydrosinomenine is much less soluble in water (0.6 per cent) than that of sinomenine, it can easily be separated by boiling the crude sinomenine hydrochloride with water. The content of the dehydrosinomenine in the plant seems to be very small. It makes up 2–3 per cent of the crude sinomenine hydrochloride.

The free base of dehydrosinomenine is precipitated from the solution of its hydrochloride by soda in fine rosettes and has m. p. 245°. The hydrochloride does not melt above 280° and the m. p. of the iodomethylate is 261°. Colour reactions of dehydrosinomenine are nearly the same with those of sinomenine, with only a marked difference that it takes yellow colour with diazobenzene sulphonic acid, instead of red. It forms also an oxime, which decomposes at 265°.

Hydrogenation of dehydrosinomenine was carried out in the hope of obtaining sinomenine or hydrosinomenine. This hope was baffled. From 21 grams of dehydrosinomenine hydrochloride, reduced with hydrogen in presence of colloidal palladium, were isolated: 7.5 grams alcohol soluble base (m. p. 245°), 1 gram alcohol insoluble base (m. p. 252°, dec.) and some brown syrup. Hydrosinomenine might have been formed here, but could not be isolated, as it is difficulty crystallisable in presence of syrupy matter, and as no salt of it is known in crystal form. The first base has the same melting point as dehydrosinomenine, so that it may be the latter, which escaped the hydrogenation. But there is some difference in its property, the iodomethylate melts at 277°, and the rotatory power is much higher (free base has $[\alpha]^{25}_{D} = +260^\circ.41$ and the hydrochloride $[\alpha]^{25.5}_{D} = +141^\circ.24$). The solubility of the hydrochloride in water is 12 per cent and that of the iodomethylate is 5 per cent.

Bromination of dehydrosinomenine, which was carried out in the exactly same manner as with sinomenine, gave bromsinomenine (m. p. 153°) only. It may, therefore, be assumed that the action of bromine on sinomenine may be oxidation at first and the dehydrosinomenine thus formed may undergo bromination, or two atoms of bromine are added to dehydrosinomenine and then the elimination of one molecule of hydrobromic acid ensues.

Destructive Oxidation and Fusion with Kali.

Destructive oxidation of sinomenine and its derivatives with potassium permanganate, chromic acid, hydrogen peroxide, nitric acid, bromine, iodine as well as with the excess of silver nitrate, ferric chloride, gold chloride, and alkaline ferricyanide gave no definite results. In most cases, only a brown syrupy matter was obtained. When nitric acid was used, oxalic acid was sometimes isolated. (found, $Ag=70.43$ per cent; $C_2O_4Ag_2$ requires $Ag=70.20$. per cent).

Careful fusion of sinomenine with caustic kali at about 200° yielded in 10 per cent yield a white crystal to the ether, after the fused mass was treated with 10 per cent ice-cold sulphuric acid. This substance melts at 169°, thus at the same degree with hemipinic acid, but it shows no property of the latter. It is almost insoluble in hot and cold water, in cold alcohol, and in dilute caustic soda. Concentrated caustic soda dissolves it in a brown solution, but the solution in dilute ammonia shows a lyrac colour, which turns brown on standing. The ferric chloride reaction in alcoholic solution is brown, but it turns purple after the addition of soda. It gives an intense nitrosoreaction. On warming it with concentrated sulphuric acid gently, smell of sulphur dioxide is produced, while no carbonisation is as yet observed.

Decomposition with benzoylanhydride.

Kondo and Ochiai showed that the decomposition of alkaloids of tetrahydro-isoquinoline group by heating them with excess of benzoylanhydride, which was so often successfully used by Gadamer and others, could be applied also to sinomenine. They obtained thus from sinomenine a nitrogen free base of m. p. 206°, which shows at least one unsaturation, revealed by the method of Wijs.

I repeated the reaction with the identical results. The new substance contains no nitrogen, it melts at 206° and seems to have the formula $C_{25}H_{20}O_5$ (found, $C=75.80$, $H=6.19$; $C_{25}H_{20}O_5$ requires $C=75$, $H=5$ per cent). Moreover I could oxidise this substance into an orthoquinone (found, $C=69.42$, $H=4.07$, $C_{25}H_{18}O_7$ requires $C=69.8$, $H=4.2$ per cent). This quinone is almost cinnober red and melts at 210°. It condences with *o*-phenylenediamine in acetic acid solution, giving yellow needle of m. p. 254°, which is to be regarded as a phenanthrophenazine (found, $N=5.50$; $C_{31}H_{22}O_5N_2$ requires $N=5.58$ per cent). This condensed product dissolves with beautiful violet colour in concentrated sulphuric acid, and takes pink colouration on the surface, when poured with concentrated hydrochloric acid.

The best condition to obtain the substance of m. p. 206° is to heat one part of sinomenine with five parts of benzoylanhydride in a strong test-tube, tightly stopped with a rubber stopper, in a glycerine bath at 160–180°, about 6 hours. After cooling, the brown mass is dissolved in chloroform and precipitated with ether. It is purified in a chloroform solution by shaking with dilute hydrochloric acid and then with soda. Yield 35 per cent. It can be recrystallised from boiling acetic acid. It gives neither ferric chloride reaction nor diazoreaction in chloroform solution. It dissolves in concentrated sulphuric acid with brown colour. Fused with kali, it gives much benzoic acid, so that the hydroxyl group of sinomenine is retained here benzoylated. Attempt to obtain oxime of this substance is not yet succeeded. Determination of unsaturation after Wijs gave the value 0.833, thus nearly equal to one double bond. After the titration, I obtained pale yellow crystal from the solution, which is very soluble in ether and shows m. p. 186°. It contains iodine as well as chlorine. The results of analysis are not concordant.

Bromination of the substance of m. p. 206° in chloroform gives hexagonal leaflet, which melts at 228°. Two derminations of bromine gave 21.24 and 21.07 per cent respectively. This would correspond to the formula $C_{18}H_{15}O_4$ Br, which requires Br$=$21.33 per cent. Then the benzoyl group might have been hydrolysed in the reaction, which is, however, very improbable. The substance of m. p. 206° was not much attacked in chloroform solution by passing dry hydrochloric acid gas for about thirty minutes.

The substance of m. p. 206° is very resistant against potassium permanganate in acetone solution. It took four days that one gram of the former decolourised 0.8 gram potassium permanganate, even when the mixture was warmed from time to time. From this fact there is some uncertainty about the existence of a vinyl side-chain in the substance of m. p. 206°, for, in that case, it must give a carboxylic acid in the above treatment. This point requires further investigation.

Distillation with Zinc Dust.

Kondo and Ochiai reported that they were successful in obtaining phenanthrene by the distillation or sinomenine with zinc dust. I have not succeeded in this point, although I tried the distillation three times under varying conditions. Once, ten grams of sinomenine hydrochloride were distilled with zinc dust in hydrogen atomosphere, and three drops of yellow liquid were obtained, which soon beautifully crystallised. The crystal became brownish on standing and a greater part of it turned out resinous after some time. Free base of sinomenine was distilled with zinc duct twice, one time in hydrogen and the other time in nitrogen atmosphere. But, in these two cases, minute crystals were recognized in the syrupy matter, but not enough to be isolated.

In every case, monomethylamine was isolated from the dilute hydrochloric acid, which was destined to absorb the basic gaseous products. A brown oil was alse obtained in minute quantity, which smelled after pyridine.

Conclusion.

From the results described above, the formula of sinomenine $C_{19}H_{23}NO_4$ may be resolved as follows.

$$C_{16}H_{13}\begin{cases} O.\,CH_3 \\ O.\,CH_3 \\ OH \\ O\ (\text{carbonyl}) \\ N\text{-}CH_3 \end{cases}$$

For the nucleous, Kondo and Ochiai assumes phenanthrene (C_{14}) in its partially hydrated form. This nucleous, combined with the remaining two carbon atoms and one nitrogen atom may constitute a condensed ring system. made of four rings, which contains a grouping somewhat like tetrahydroisoquinoline, just as morphine or apomorphine does.

This conclusion may be correct, for, although I can not yet take out phenanthrene from sinomenine by the distillation with zinc dust, yet the substance of m. p. 206° seems to be a derivative of phenanthrene, giving an orthoquinone, which shows similar character to that of phenanthrene quinone.

The substance of m. p. 169°, obtained from sinomenine by fusion with kali is now under closer investigation. It is hoped that the determination of the constitution of this substance will throw some light on the constitution of sinomenine itself.

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[Received, September, 8th, 1924]

On Vitamin C in the Green Tea.

By Masataro Miura, and Michiyō Tsujimura.

The authors observed that green tea has a fairly high antiscorbutic potency, while black tea almost lacks this power. This difference may be considered to be caused by the different processes of manufacture of these teas. In the manufacture of green tea the fresh leaves are withered by steaming, and taken in a low wooden flame with paper bottom over the charcoal fire, spreading and drying by rolling over and over for 2–3 hours, so as to reduce its oxidation and to retain the green color as much as possible. But in the manufacture of black tea the cellular tissues of the fresh leaves are first broken mechanically, and exposed to the direct sun light for some hours and then are fermented at a moderately high temperatures, completely converting green colour into brown on account of oxidation in the process.

As the antiscorbutic potency is most easily destroyed by oxidation at high temperature so it is quite natural that the authors found the potency is nearly absent in black tea.

The method used by the authors is followed to the one which is schemed by the member of the Lister Institute of Preventive Medicine, London. Guinea pigs of 270-330 grammes are fed with the mixture of equal volumes of oats and wheat bran ad libitum, and 40–50 c.c. of the milk autoclaved at 120° for an four per day as the basal diet for twelve days, and then the infusion of the tea to be tested is added into the above foods. The tea is always weighed and extracted with a few c.c. of hot water of 60°–70° for 5–7 minutes whenever the impression is required, and to the freshly prepared infusion a few drops of the autoclaved milk mentioned above is added and the mixture is given to the animals by means of forced feeding. The noxious effects of tannin present are modified by the addition of the milk.

Thus the infusion obtained from one gram of the green tea of last year sold in stores here has been proved completely to prevent the animals from scurvy for more than 60 days, and sometimes no scorbutic sign is shown for 108 days.

It should be kept in mind that the weight of the animals may be decreased when fed with such a substance containing a considerable amount of caffeine and tannin besides vitamin C, even the amount of vitamin C given is increased by a more addition of the substance, as the influence of these intermixtures thus be increased, and also the terms of existence of the animals may be shortened. For this reason, the determination of its antiscorbutic value always requires the *post mortum* examination.

The antiscorbutic potency of the green tea is proved not due to tannin and caffeine, and the experimental results as to the antiscorbutic value of both new and old teas under investigation are shown in the following, provided that all of these contain 4–5% of moisture.

New tea	0.4–0.6 g. per day.
One year stored tea	0.75 „ „ „
Two years „ „	1.00 „ „ „
Four years „ „	negligible „ „

It is also noticed that even an old tea, in case it has a comparatively high lusture and aroma, gives a fairly high potency, and that the potency of the coarse tea (Băn-Chă) though manufactured in this year, is not much significant.

Studies on the Colloidal Substances in Alcoholic Beverages with the Interferometer.

By Teizō Takahashi and Hōbun Ōmachi.

The Löwe's interferometer was used for the determination of the colloidal substances in alcoholic beverages, especially in various beers and beer worts by Adler and Luers (Zeit f. d. Ges. Brauw. 1916 Nr. 3–Nr. 6.). No consideration was however given as to the relation existing between the so called "Colloid Number" measured by the interferometer and the analytical percentage of the actual colloidal substances present.

The authors investigated how much an accuracy should be obtained with the instrument using very common colloidal substances such as dextrin and peptone, and tried to find a more suitable substance for removing the colloidal substances than animal charcoal using blood charcoal, barium phosphate etc. for the investigation but these gave no satisfactory result. After all the animal charcoal of the Maerck's brand was found to be the best and most suitable for this purpose.

In the determination of the colloidal substances in the beer, it was diluted with ten volumes of distilled water, 0.5 g of the animal charcoal was added to 50 c.c. of the sample and they noticed that the "Colloid Number" thus obtained is almost equal to (hundred times of) the number of grams of the actual colloids present in 100 c.c. of the sample solution, assuming dextrins and proteins were the main colloidal substances in the beverage.

The following table shows according to the authors' experiments the relation between the "Colloidal Number" and the actual percentage of the colloids present.

Beer	No. 1	No. 2	No. 3	No. 4	No. 5	No. 6	No. 7
Dextrin	2.07	2.07	2.11	2.77	2.16	1.87	1.89
Protein	0.12	0.126	0.13	0.09	0.13	0.11	0.119
Sum	2.19	2.19	2.24	2.86	2.26	1.93	2.00
"Drum Number"	735	760	771	1023	753	719	780
"Colloid Number"	2.30	2.28	2.35	2.77	2.26	2.29	2.30

In the case of "Sake," having the same dilution as that in the case of the beer, a less amount of the charcoal was sufficient for the purpose, thus 0.003 g of the charcoal was suitable for "Sake" having a comparatively smaller "drum number" as 1085, while a larger amount of the charcoal, say 0.005 g was required for one which having a larger "drum number" as 1291 or 1331.